

REMARKS

Claims 5-10, 21, 23, 24, and 26-29 are pending in this application. Claims 5 and 21 have been amended to clarify the claim. No new matter has been added.

The issues outstanding in this application are as follows:

- Claims 5-10, 21, 23, 24 and 26-29 were rejected under 35 U.S.C. §103(a), in which the Examiner alleges that the claimed subject matter is unpatentable over Teng et al. in view of Britigan, Morianga Milk Inc. (JP 07-233086) and De Lacharriere et al.
- Claims 5-10, 21, 23, 24 and 26-29 were rejected under 35 U.S.C. §103(a), in which the Examiner alleges that the claimed subject matter is unpatentable over Teng et al. in view of Nuijens et al., Enk et al., Database WPI AN 95-340208 and Penco et al. and further in view of Morinaga Milk Inc. (JP 07-233086).

Applicants respectfully traverse the outstanding rejections and objections, and applicants respectfully request reconsideration and withdrawal thereof in light of the amendments and remarks contained herein.

- I. Teng et al. in combination of Britigan et al., Morinaga Milk Inc., and De Lacharriere et al.

Claims 5-10, 21, 23, 24 and 26-29 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over the primary reference Teng et al. in combination of the above-listed references.

The Examiner states that Teng et al. teaches a method of treating dermal inflammatory disorder comprising the step of administering a pharmaceutically effective amount of lactoferrin product. The Examiner also states that Teng et al. does not teach the treatment of the particular dermal disorder or the employment of biological analog or fragments of lactoferrin. The Examiner states that Britigan teaches that lactoferrin is known to be useful as an anti-inflammatory agent and that Morinaga Milk Inc. teaches that lactoferrin or its derivatives are known to be useful for treating various skin disorders. The

Examiner also states that De Lacharrier et al. teaches that TNF antagonists, lactoferrin, are known to treat or prevent skin inflammation. Applicants traverse.

The MPEP sets forth the guidelines to establish a *prima facie* case of obviousness under 35 U.S.C. § 103 (MPEP § 2143.3). Three basic criteria must be met to establish a *prima facie* case of obviousness. The three criteria are:

- 1) a suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings;
- 2) a reasonable expectation of success; and
- 3) the prior art references must teach or suggest all the claim limitations.

In view of the above criteria, Applicants assert that the Office has not established a *prima facie* case of obviousness to reject the claims under 35 U.S.C. § 103 in light of the above criteria. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438, (Fed. Cir. 1991). A *prima facie* case necessitates disclosure of the source for either a suggestion or motivation to modify a reference to produce the present invention, and a reasonable expectation of success of producing the present invention. A *prima facie* case must be established by evidence rather than conjecture. *Ex parte Yamamoto*, 57 USPQ2d 1382, 1383, 1384 (CCPA 2000). In the present case, it is mere conjecture on the part of the Office that one of skill in the art would be able use the lactoferrin composition in Teng et al. in combination with the lactoferrin compositions described in Britigan et al., Morinaga Milk Inc., and the TNF α antagonists described in De Lacharriere to develop the lactoferrin composition of the present invention to treat an allergen-induced inflammatory response.

The present invention is drawn to the use of lactoferrin to prevent or treat an allergen-induced inflammatory response. An allergen is an innocuous agent; it is not a pathogen. The below definitions are provided for the Examiner's convenience.

Allergens are defined as antigens that elicit hypersensitivity or allergic reactions. (Immunobiology 4th Ed., page 593, 1999).

An allergic reaction is a response to innocuous environmental antigens or allergens due to pre-existing antibody or T cells. (ImmunoBiology 4th Ed., page 594, 1999).

Hypersensitivity reactions are immune responses to innocuous antigens that lead to symptomatic reactions upon re-exposure. (ImmunoBiology 4th Ed., page 602, 1999).

Infection is invasion by and multiplication of pathogenic microorganisms in a body tissue. (American Heritage College Dictionary 3rd Ed., page 696, 1997).

Those of skill in the art realize that the mechanisms involved in an allergen-induced immune response differ from an immune response resulting from an insult by a pathogenic agent, such as bacteria or viruses (See 1.132 Declaration, paragraphs 3-6). Inflammation that occurs via a pathogenic agent is typically a result of endotoxin toxicity. Endotoxins are toxins that are released from the pathogen. An endotoxin is not an innocuous agent; it is toxic to the cell and triggers phagocytes to release cytokines that produce local or systemic symptoms. An allergen-induced inflammatory response results from the immune system responding to an innocuous agent.

Applicants assert that Teng et al., Britigan et al., and Morinaga Milk Inc. do not teach or suggest the use of lactoferrin to treat an allergen-induced inflammatory response. The present application, on page 3, lines 20-21, indicates that lactoferrin inhibits allergen-induced inflammation that is not induced by an endotoxin, such as lipopolysaccharide (LPS). Teng et al. teaches the use of lactoferrin as a treatment for **antibacterial and antiviral infections** (see page 4, lines 21-30 and page 13, lines 1-5). Britigan et al. also teaches the use of lactoferrin to treat **bacterial infections** via scavenging free radicals that are produced by phagocytosis. In fact, Britigan et al. further suggests that lactoferrin may play a role in ameliorating LPS-induced toxicity (see page 151, last sentence of summary). Morinaga Milk Inc. also teaches the **antimicrobial effects** of lactoferrin. Thus, Applicants assert that the combination of Teng et al., Britigan et al. and Morinaga Milk Inc. teach the **antimicrobial activity of lactoferrin** (lactoferrin's activity against a pathogen), however, the references do not teach or suggest the use of lactoferrin to treat an allergen-induced immune response (lactoferrin's activity against an innocuous agent).

De Lacharriere is cited for teaching the use of TNF α antagonists in pharmaceutical compositions. De Lacharriere does not describe that lactoferrin is a TNF antagonist. In fact,

the term “TNF α antagonists” is defined purely in functional terms, see column 3 lines 4-10 of the De Lacharriere patent. It is stated that “all substances capable of inhibiting the release and/or synthesis and/or receptor binding of ...TNF alpha” are considered “TNF α antagonists.” Without teaching the structures of potential TNF α antagonists, no one in the art would know how to select a candidate from millions of natural and recombinant biological molecules in order to test for its ability to inhibit TNF α production. Such a general statement in De Lacharriere cannot be fairly construed as providing a suggestion for one skilled in the art to select lactoferrin, and specifically, to test its ability to inhibit TNF α production in dermal cells, and to conduct the test under the particular condition that the mammal has been inflicted with an allergen. (See 1.132 Declaration, paragraph 8)

Applicants contend that the teachings of Teng et al., Britigan et al., Morinaga Milk Inc. and De Lacharriere alone or in combination do not teach nor suggest using lactoferrin to treat an allergen-induced inflammatory response. These references teach the use of lactoferrin to inhibit LPS toxicity, which LPS toxicity is not involved in an allergen-induced response. (See 1.132 Declaration, paragraphs 7-8 and 10) Thus, with the lack of teaching or suggestion, Applicants assert that the references do not meet the basic requirements of a *prima facie* case of obvious and respectfully request that the rejection be withdrawn.

II. II. Teng et al. in combination of Nuijens et al., and Enk et al, Database WPI AN 95-340208, and Penco et al and in further view of Morinaga Milk Inc.

Claims 5-10, 12-14 and 21-25 stand rejected under 35 U.S.C. § 103 (a) as allegedly being unpatentable over the primary reference Teng et al. in combination of the above-listed references, all of which are of record. Applicants traverse.

The MPEP sets forth the guidelines to establish a *prima facie* case of obviousness under 35 U.S.C. § 103 (MPEP § 2143.3). Three basic criteria must be met to establish a *prima facie* case of obviousness. The three criteria are:

- 1) a suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings;

- 2) a reasonable expectation of success; and
- 3) the prior art references must teach or suggest all the claim limitations.

As explained in the section above, the primary reference, Teng et al., fails to teach or suggest the use of lactoferrin to treat an allergen-induced inflammatory response. Applicants also contend that the secondary references do not teach or suggest that lactoferrin can be used to treat allergen-induced inflammatory responses. (See 1.132 Declaration, paragraphs 7-10).

Nuijens et al. reports that lactoferrin suppresses IL-1 and TNF- α release from monocytes in response to LPS from Gram-negative bacteria. See last paragraph at page 287 that is cited by the Examiner. Nuijens does not teach or suggest that lactoferrin suppresses IL-1 or TNF- α production from dermal cells in response to an allergen, which is mediated through an LPS independent pathway. (See 1.132 Declaration, paragraph 9) As such, Nuijens et al. is not on point and adds nothing to the notion of using lactoferrin for treatment of dermal inflammation, and more specifically allergen-induced inflammation.

Applicants believe that the Examiner may have cited the same reference twice. AN 95-340208 and Morinaga Milk Inc. are the same Japanese Publication JP07233086A. Thus, JP07233086A teaches the preparation and use of a lactoferrin composition that confers antimicrobial activity, which again relates to LPS pathway as stated and distinguished in the specification. As such, JP07233086A fails to appreciate the anti-allergen activity of lactoferrin and fail to describe other required elements of the invention. (See 1.132 Declaration, paragraph 7)

Enk et al. and Penco et al. report in vitro studies on two cytokines, namely IL-1 β and TNF- α . Neither reference fairly suggests the relevance, if any, of the in vitro test to an in vivo application of lactoferrin.

In light of the above arguments, Applicants assert that the Office has not established a *prima facie* case of obviousness to reject the claims under 35 U.S.C. § 103. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438, (Fed. Cir. 1991). A *prima facie* case necessitates disclosure of the source for either a suggestion or motivation to modify a reference to produce the present invention, and a reasonable expectation of success of producing the present invention. A

prima facie case must be established by evidence rather than conjecture. *Ex parte Yamamoto*, 57 USPQ2d 1382, 1383, 1384 (CCPA 2000). In the present case, it is mere conjecture on the part of the Office that one of skill in the art would be able use the lactoferrin composition in Teng et al. in combination with the lactoferrin compositions described in Nuijens et al., JP07233086A and the cytokine teachings of Enk et al., and Penco et al. to develop the lactoferrin composition of the present invention to treat an allergen-induced inflammatory response. Applicants contend that the teachings of Teng et al., Nuijens et al., JP07233086A, Enk et al., and Penco et al. do not teach nor suggest using lactoferrin to treat an allergen induced inflammatory response. These references teach the use of lactoferrin to inhibit LPS toxicity, which LPS toxicity is not involved in an allergen induced response. (See 1.132 Declaration, paragraph 10) Thus, with the lack of teaching or suggestion, Applicants assert that the references do not meet the basic requirements of a *prima facie* case of obvious.

Thus, with the lack of teaching or suggestion, Applicants assert that the references do not meet the basic requirements of a *prima facie* case of obvious and respectfully request that the rejection be withdrawn.

CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to pass this application to issue.

Applicant believes no fee is due with this response. However, if a fee is due, please charge our Deposit Account No. 06-2375, under Order No. 10211629 from which the undersigned is authorized to draw.

Dated: August 21, 2003

Respectfully submitted,

By 

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